What is claimed:

1. A method for modulating the production of Aβ11-40/42 peptide fragments comprising contacting a sample or cell containing a beta-site APP-cleaving enzyme 1 (BACE1) and an amyloid precursor protein (APP) with a BACE1-modulating agent such that production of Aβ11-40/42 is modulated.

2. The method of claim 1, wherein the modulation is inhibition of Aβ11-40/42 peptide formation.

3. The method of claim 1, wherein the contacting is *in vivo*.

4. The method of claim 1, wherein the contacting is *in vitro*.

5. The method of claim 1, wherein the BACE1-modulating agent is an anti-BACE1 antibody or a BACE1 antisense molecule.

6. A method for identifying a compound which inhibits beta-site APP-cleaving enzyme 1 (BACE1) expression or activity comprising:

   a) incubating components comprising the compound, BACE1 polynucleotide or polypeptide, and an amyloid precursor protein (APP) under conditions sufficient to allow the components to interact; and

   b) measuring the production of a BACE1 specific enzymatic product.

7. The method of claim 6, wherein the compound is a peptide or a small molecule inhibitor.

8. The method of claim 6, wherein the BACE1 polynucleotide or polypeptide is expressed in a cell.

9. The method of claim 6, wherein the BACE1 specific enzymatic product includes a sequence of Aβ11-40/42.

10. A compound identified by the method of claim 6.

11. The compound of claim 10 in a pharmaceutically acceptable carrier.

12. A method for diagnosing a subject having or at risk of having an Aβ11-40/42 peptide accumulation disease, the method comprising:

measuring the amount of beta-site APP-cleaving enzyme 1 (BACE1) in a biological sample from the subject; and

comparing the amount BACE1 with a normal standard value of BACE1, wherein a difference between the measured amount and the normal sample or standard value provides an indication of the diagnosis of Aβ11-40/42.

13. The method of claim 12, wherein the biological sample is blood, serum, cerebrospinal fluid or central nervous system (CNS) tissue.

14. The method of claim 12, wherein the difference is an increase in BACE1.

15. The method of claim 12, wherein the amount BACE1 is measured by detecting the amount of a polynucleotide encoding BACE1.

16. The method of claim 15, wherein the polynucleotide is mRNA.

17. The method of claim 12, wherein the amount of BACE1 is detected by contacting the sample with an agent that specifically binds to a BACE1 polypeptide.

18. The method of claim 17, wherein the agent is an antibody.

19. The method of claim 17, wherein the Aβ11-40/42 accumulation disease is Alzheimer's disease.

20. The method of claim 12 further comprising detecting the level of an APP fragment, wherein an increase in the presence of the fragment is indicative of Alzheimer's disease.

21. The method of claim 20, wherein the APP fragment is an Aβ1-40, Aβ1-42, Aβ11-40, or Aβ11-42 fragment.

22. The method of claim 21, wherein the fragments are detected by contacting the sample with an agent the specifically binds to an Aβ1-40, Aβ1-42, Aβ11-40, or Aβ11-42 fragment.

23. The method of claim 22, wherein the agent is an antibody.

24. A method for diagnosing a subject having or at risk of having Alzheimer's disease, the method comprising:

measuring Aβ11-40/42 in a biological sample from the subject; and

comparing the amount of Aβ11-40/42 with a normal sample or standard value of Aβ11-40/42, wherein a difference between the amount in the normal sample or standard value is indicative of a subject having or at risk of having Alzheimer's disease.

25. The method of claim 24, wherein the biological sample is cerebrospinal fluid, central nervous system (CNS) tissue, serum or blood.

26. The method of claim 24, wherein the difference is an increase in Aβ11-40/42 and the increase is indicative of a disposition for Alzheimer's disease.

27. The method of claim 24, wherein the difference is a decrease in Aβ11-40/42.

28. The method of claim 24, wherein the amount of Aβ11-40/42 is detected by contacting the sample with an agent that specifically binds to Aβ11-40/42.

29. The method of claim 28, wherein the agent is an antibody.

30. A transgenic non-human animal having a transgene disrupting expression of BACE1, chromsomally integrated into the germ cells of the animal, and having a phenotype of reduced Aβ peptide as compared with a wild-type animal.

31. The transgenic non-human animal of claim 30, wherein the animal is an avian, bovine, ovine, piscine, murine, or porcine species.

32. The transgenic non-human animal of claim 30, wherein the animal is heterozygous or homozygous for the disruption.

33. The transgenic non-human animal of claim 30, wherein the transgene comprises a BACE1 antisense polynucleotide.

34. A method for identifying an agent that modulates the expression or activity of BACE1, said method comprising:

administering an agent to be tested to an organism; and

comparing the phenotype of the organism contacted with the agent with that of a BACE1-knockout organism not contacted with the agent, whereby a phenotype substantially equal to the BACE1-knockout organism is indicative of an agent that modulates BACE1 expression or activity.

35. The method of claim 34, wherein the organism is a transgenic organism.

36. The method of claim 35, wherein the transgenic organism is transgenic for overexpression of BACE1; APP expression; $A\beta1-40$, $A\beta1-42$, $A\beta11-40$, $A\beta11-42$ expression; or a combination thereof.

37. The method of claim 34, wherein the expression of BACE1 is detected by measuring the amount of BACE1 polynucleotide in the organism.

38. The method of claim 37, wherein the BACE1 polynucleotide is RNA or DNA.

39. The method of claim 34, wherein the activity of BACE1 is detected by measuring BACE1 cleavage of APP.

40. The method of claim 34, wherein the phenotype of the organism is associated with Alzheimer's disease.

41. A kit useful for the detection of an Aβ11-40/42 accumulation disorder comprising carrier means containing therein one or more containers wherein a first container contains a nucleic acid probe that hybridizes to a nucleic acid sequence BACE1 or an antibody probe specific for BACE1 or Aβ11-40/42.

42. The kit of claim 41, wherein the probe comprises a detectable label.

43. The kit of claim 41, wherein the label is selected from the group consisting of radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, and an enzyme.

44. A method for predicting the therapeutic effectiveness of a compound for treating Alzheimer's disease in a subject comprising measuring the accumulation of AB11-40/42 peptide fragments in the subject or the level of BACE1 polynucleotide or polypeptide before and after treatment with the compound,

wherein a decrease in accumulation of peptide fragments or a decrease in the level of BACE1 polynucleotide or polypeptide after treatment is indicative of a compound that is effective in treating the disease.

45. A substantially purified antibody that specifically binds a beta-site APP-cleaving enzyme 1 (BACE1) polypeptide or an epitopic determinant thereof.

46. The antibody of claim 45, which is present in an antiserum.

47. The antibody of claim 45, which comprises polyclonal antibodies.

48. The antibody of claim 45, which is a monoclonal antibody.

49. The antibody of claim 45, wherein the epitopic determinant comprises amino acid residues 46 to 164 of BACE1.

50. A method of detecting a beta-site APP-cleaving enzyme 1 (BACE1) polypeptide in a sample, the method comprising contacting the sample with the antibody of claim 45 under conditions that allow specific binding of the antibody to BACE1 or an epitopic determinant thereof, and detecting specific binding of the antibody to a component of the sample.

51. The method of claim 50, wherein the sample is a tissue sample, which is obtained from a subject.

52. The method of claim 51, wherein the tissue sample is a brain tissue sample.

53. The method of claim 51, wherein the subject has or is suspected of having a disorder associated with an accumulation of amyloid plaques.

54. The method of claim 53, wherein the disorder is Alzheimer's disease.

55. The method of claim 50, wherein the antibody comprises a detectable label, and wherein said detecting specific binding comprises detecting the label.

56. The method of claim 50, further comprising contacting the sample with a reagent that specifically binds the antibody, wherein detecting specific binding of the antibody comprises detecting specific binding of the reagent.